I hereby certify that this correspondence is being electronically filed in the United States Patent and Trademark Office on October 31, 2008.

Frank C. Eisenschenk, Ph.D., Patent Attorney

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322 AND UNDER 37 CFR 1.323
Docket No. ARS.104

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Amanda Proudfoot, Maria Kosco-Vilbois, Tracy Handel
Issued	:	September 16, 2008
Patent No.	:	7,425,324
For	:	Antagonists of MCP Proteins

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE) AND
UNDER 37 CFR 1.322 (APPLICANT MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:	**Application Reads:**
Title page, Assignee Item (73):	Notice of Recordation of Assignment Document, Reel/Frame 015987/0741:
"Laboratoires Serono SA, Coinsins, Vaud (CH)"	--Laboratoires Serono SA, Coinsins, Vaud (CH); The Regents of the Univcrsity of California, Oakland, California--

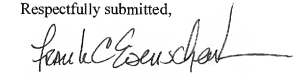
Column 14, line 2:	Page 26, line 13:
"*E. coli* i"	--*E. coli*--
Column 17, line 4:	Page 32, line 14:
"C57BU6"	--C57BL/6--
Column 17, line 32:	Page 33, line 9:
"C57 BU6NCrlBR"	--C57 BL/6NCrlBR--.

A true and correct copy of pages 26, 32 and 33 of the specification as filed and a copy of the Notice of Recordation of Assignment Document which support Applicants' assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

The fee of $100.00 was paid at the time this Request was filed. The Commissioner is also authorized to charge any additional fees as required under 37 CFR 1.20(a) to Deposit Account No. 19-0065.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



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FCE/ps

Attachments: Copy of pages 26, 32 and 33 of the specification
Copy of Notice of Recordation of Assignment Document

sequence, called MCP-1WT*, was cloned and expressed in *E. coli* by making use of a plasmid based on the pET3 plasmid (Paavola CD et al, 1998) as a protein containing 77 residues (fig. 1A; SEQ ID NO: 2).

The plasmid expressing MCP-1WT* was then further mutagenized by cloning a PCR fragment encoding for two Alanines instead of Arginine and Lysine in positions 41 and 42 of human MCP-1 precursor (position 18 and 19 in the mature protein), in order to generate the MCP-1 mutant MCP-1WT*2A, having the same length and purification features of MCP-1WT* (fig. 1; SEQ ID NO: 3).

All constructs were obtained and controlled by standard molecular biology technologies (PCR mutagenesis and amplification, DNA sequencing, restriction digestion) and maintained in the DH5alpha strain of *E. coli* during the cloning process. The coding sequences were chosen in order to have an optimal codon usage for the expression in *E. coli* (Kane JF, 1995).

The pET3-based plasmids encoding for MCP-1WT* and MCP-1WT*2A were then transferred in an *E. coli* BL21(pLys)-derived strain called TAP302 and the resulting strains were used the recombinant expression of the MCP-1 mutants as described (Paavola CD et al, 1998). This protocol includes the use of aminopeptidase to remove the N-terminal methionine, thus obtaining recombinant MCP-1 mutants having the same length of the natural mature form (76 amino acids; fig. 1B). The identity of the recombinant proteins was verified by mass spectrometry.

Chromatographic assays of MCP-1WT and MCP-1WT*2A.*

MCP-1WT* and MCP-1WT*2A were loaded either onto a Heparin Sepharose column or onto a SP Sepharose cation exchange column. In both cases the column

The mouse ear-swelling test to measure contact hypersensitivity was performed as previously described (Garrigue JL et al., 1994). Briefly, mice were pre-sensitized topically by applying 25 µl of 0.5% 2,4-dinitrofluorobenzene (DNFB; Sigma Chemical Co.) solution in acetone/ olive oil (4:1) to the shaved abdomen. Five days later, 20 µl of 0.2% DNFB in the same vehicle was applied to the right ears, and vehicle alone to the left ears. Mice were treated daily from Day 5 to 9 with an intraperitoneal administration of either 0.5 mg/kg (10 micrograms/mouse) of MCP-1WT* or PBS only in the control group. The first treatment was administered 1 hour prior to the DNFB challenge. Ear thickness was measured with a dial thickness gauge (Mitutoyo Corp.), and ear swelling was estimated by subtracting the pre-challenge from the post-challenge value, and by further subtracting any swelling detected in the vehicle-challenged contralateral ear.

Bleomycin Induced Lung Fibrosis Model

C57BL/6 female mice received bleomycin (3.75 U/kg in 25 µl PBS) intra-tracheally (day 0). One hour after the instillation of bleomycin, test animals received intraperitoneally either 0.25 mg/kg MCP-1WT*2A in 0.2 ml PBS or only 0.2 ml PBS. This treatment was given daily and continued for 10 days. The body weight loss and percentage of mortality were recorded daily. At day 10, all mice were sacrified by CO_2 asphyxiation. Four lung lobes were placed at –80°C for measurement of hydroxyproline levels as an indication of collagen deposition as well as one lobe processed for histological determination of pulmonary fibrosis. Total lung collagen was determined by the analysis of hydroxyproline. Briefly, lungs were homogenized in Tris-HCl (pH 7.6) with a Tissue Tearor followed by incubation in Amberlite overnight at 115°C. Citrate/acetate buffer, isopropanol, chloramine-T and DAB solutions were added to the samples and left for 30 minutes at 60°C. Samples were cooled at room temperature for

10 minutes and read at 560 nm on spectrophotometer. Pulmonary fibrosis was also determined histologically by fixation of the right lung lobe in 10% Formalin, followed by embedding in paraffin, sectioning, and staining with Masson's trichrome solution. Histological changes were examined by light microscopy. Morphological evaluation of bleomycin-induced lung inflammation and fibrosis was performed using a semi-quantitative scoring method, calculating the percentage of the fibrotic area.

Experimental Autoimmune Encephalomyelitis (EAE) Model

Female mice (8-week old; C57 BL/6NCrlBR strain; 18-22 grams of weight) were immunized at day 0 by injecting 0.2 ml of an emulsion containing the MOG_{35-55} peptide (200 micrograms) and Mycobacterium tuberculosis (500 micrograms) in Complete Freund's Adjuvant (CFA; Difco Lab.) subcutaneously in the left flank. Immediately afterwards, pertussis toxin (500 nanograms in 400 microliters of a buffer containing 0.5 M NaCl, 15 mM Tris (pH 7.5), 0.017% Triton X-100) was administered intraperitoneally. On day 2 the animals were given a second intraperitoneal injection of the same solution containing pertussis toxin. On day 7, the mice were administered a second dose of MOG_{35-55} peptide (200 micrograms) in CFA injected subcutaneously in the right flank. This procedure results in disease onset at approximately day 18-20, with the appearance of a progressive paralysis, arising from the tail and progressively ascending up to the forelimbs.

The treatment was started for each animal at experimental day 7 (approximately 1-3 days before the usual occurrence of the disease) and continued for 21 consecutive days. Starting from day 7, the animals were examined individually for the presence of paralysis by means of a clinical score as follows:

0 = no sign of disease

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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Washington, D.C. 20231

MAY 10, 2005

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UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, MAIL STOP: ASSIGNMENT SERVICES DIVISION, P.O. BOX 1450, ALEXANDRIA, VA 22314.

RECORDATION DATE: 03/31/2005

REEL/FRAME: 015987/0741
NUMBER OF PAGES: 4

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
HANDEL, TRACY

DOC DATE: 12/12/2004

ASSIGNEE:
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SERIAL NUMBER: 10510658
PATENT NUMBER:

FILING DATE:
ISSUE DATE:

TITLE: NOVEL ANTAGONISTS OF MCP PROTEINS

MARY BENTON, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,425,324

APPLICATION NO.: 10/510,658

DATED : September 16, 2008

INVENTOR : Amanda Proudfoot, Maria Kosco-Vilbois, Tracy Handel

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Cover page,
Item (73), Assignee, "Laboratoires Serono SA, Coinsins, Vaud (CH)" should read --Laboratoires Serono SA, Coinsins, Vaud (CH); The Regents of the University of California, Oakland, California--.

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Line 4, "C57BU6" should read --C57BL/6--.
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